Dialysate Volume Requirements to Normalize Serum Phosphorus Concentration During Frequent Nocturnal Haemodialysis Based on a Modified Pseudo-One Compartment Kinetic Model

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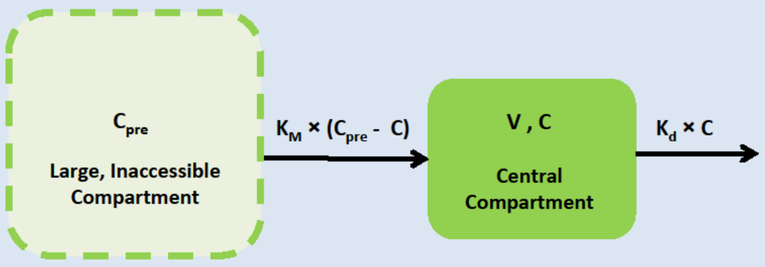
Introduction and Objective

Frequent nocturnal haemodialysis (HD) is a high dose prescription option that can use low dialysate flow rates to normalize serum phosphorus concentration; however, the volume of dialysate required per treatment to achieve such a goal remains unclear. Daugirdas (Semin Dial 2015) recently reported that 18-30 hours per week can normalize serum phosphorus concentration, but such recommendations depend on the total dialysate volume prescribed. A definition of the total dialysate volume requirements for such purposes may improve the design of novel dialysis delivery systems.

Certain, but not all, studies suggest that serum phosphorus concentration can increase, i.e. rebound, during the HD treatment, and recent work suggests that the rebound in serum concentration is due to an increase in intracellular phosphorus concentration (Lemoine et al, J Am Soc Nephrol 2015). We compared estimates of the dialysate volume required per treatment to normalize serum phosphorus concentration without oral phosphorus binding agents during frequent nocturnal HD using a conventional pseudo-one compartment (POC) model and a modified POC model with an increasing phosphorus concentration in the inaccessible, i.e. intracellular, compartment (at 3.5% per hour).

Methods

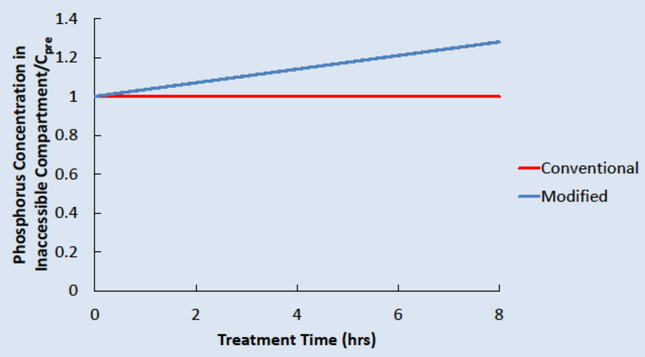
Dialysate volumes per treatment required to achieve a normalized serum phosphorus concentration of 1.6 mmol/L (5.0 mg/dL) were determined during 4, 5 and 6 treatments (Tx) per week (for both 6-hr and 8-hr Tx) using conventional and modified POC models. The conventional POC model has been described previously (Agar et al, Clin J Am Soc Nephrol 2011) and is shown schematically below.



Pseudo one-compartment (POC) model

C_{pre}: Predialysis serum phosphorus concentration
C: Serum phosphorus concentration
K_M: Phosphorus mobilization clearance
V: Volume of central compartment
K_d: Dialyzer phosphorus clearance

The POC model is a simplified two compartment model where the inaccessible compartment has been assumed to be very (infinitely) large such that the concentration within that compartment remains constant at C_{pre}. The modified POC model is identical except that the concentration within the inaccessible compartment was assumed to increase linearly during the treatment at a rate of 3.5% per hour. This is shown schematically below.



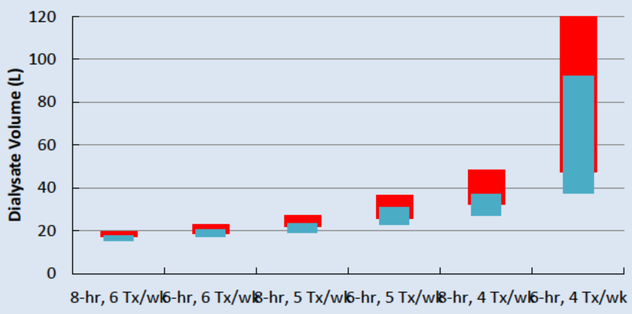
The mathematical details for using the conventional POC model have been previously reported (Leypoldt et al, Int J Artif Organs 2012; Leypoldt et al; Nephrol Dial Transplant 2014). The following parameters were fixed for these model predictions: dialyzer mass transfer-area coefficient for phosphorus 40% of that of urea (Xenium 190 dialyzer), blood flow rate of 300 mL/min, hematocrit of 30%, weekly fluid removal of 9 L.

Results

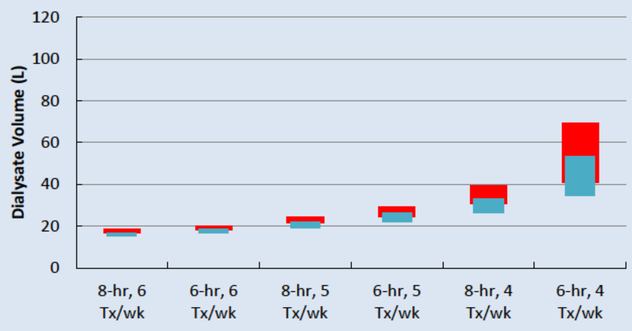
Dialysate Volumes Per Treatment Required to Normalize Serum Phosphorus Concentration

Boxes show the interquartile range of calculated dialysate volumes for phosphorus mobilization clearances between 65 and 116 mL/min (Leypoldt et al, Kidney Int 2013). Results for the conventional POC model are shown in the red boxes and those for the modified POC model are shown in the blue boxes. Calculated volumes greater than 120 L are shown as 120 L.

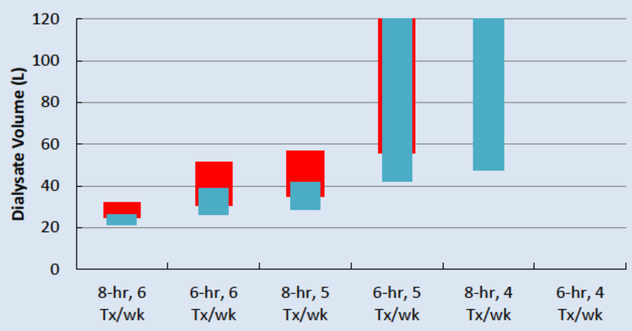
For postdialysis V = 10 L and dietary protein intake = 70 g/day



For postdialysis V = 15 L and dietary protein intake = 70 g/day



For postdialysis V = 10 L and dietary protein intake = 90 g/day



Discussion Summary

- ✓ Calculated dialysate volumes per treatment required to normalized serum phosphorus during frequent, nocturnal HD were dependent on the number of treatments per week and treatment time.
- ✓ Higher central compartment volumes (i.e., larger patients) per se minimally reduced the required dialysate volume.
- ✓ Higher dietary protein intake substantially increased the required dialysate volume.
- ✓ If the inaccessible (intracellular) phosphorus concentration increases during a HD treatment, the required dialysate volume is modestly reduced.

Conclusions

Flexibility of prescribing frequent, nocturnal HD requires a range of dialysate volumes. Dialysis delivery systems designed for frequent, nocturnal HD should provide for large dialysate volumes to allow prescription flexibility.

Once validated in a clinical trial, a pseudo one-compartment model will allow individualization of prescriptions during frequent, nocturnal HD to normalize serum phosphorus concentration without a need for oral binding agents.

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